of patients who—having been treated in the cabinet and recovered sufficiently to have a partly separate existence on, say, one-sixth or less of the normal breathing capacity—have had to be re-admitted to hospital when a minor lower respiratory infection has resulted in severe underventilation with coma or near coma. There has never been an occasion in my experience where in such a crisis a patient has had to have tracheostomy. They have in every instance been restored to their normal condition with skilful chest physiotherapy after a short time in the modern pattern of the cabinet. Indeed, where there were gross bronchial secretions and atelectasis there has never been a failure, even in the days before I had developed, together with the engineers of the Cape Engineering Company, of Warwick, our rotatable cabinet.¹ Experienced, and I might add intelligent, patients view with horror the idea that on each occasion when such a crisis occurs—and it may involve some frequently—they would be subjected to tracheostomy or intubation. They also view with fear and distaste the idea that they should have a permanent tracheostome.

I am, myself, a strong advocate of the continued use of the cabinet for the type of case which can effectively and comfortably be treated in it, and these cases were very numerous when polio was epidemic. However, I hope it will be clear from the foregoing remarks that I am not prejudiced against other methods; indeed, in 1951² I advocated the use of tracheostomy in bulbo-respiratory polio with the practice of such techniques as were then being studied in certain centres in the U.S.A. Furthermore, the pioneer work on I.P.P.V. by the Danes in 1952 was studied in Denmark during the polio epidemic by Dr. Brian Sellick and myself, and we made strong advocacy to interested branches of the profession and to the Ministry of Health to introduce the techniques in this country and to develop apparatus. The Ministry of Health working party (Breathing Machines Group), of which I am chairman, did much work in the development of pumps and other devices for I.P.P.V. in the years following the Danish experience. Some of these respirators have given many years of satisfactory service in total respiratory paralysis. I might add that the working party also recommended the continued use of the cabinet respirator.—I am, etc.,

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Febrile Convulsions

SIR,—I am grateful to Professor J. H. Hutchison for his friendly review of the second edition of my book *Common Symptoms of Disease in Children* (16 August, p. 406). He criticizes my recommendation (directed mainly at family doctors) that a lumbar puncture should be performed on every child with a febrile fit.

My reasons for the recommendation lie in the difficulty of being certain that the diagnosis is correct. I maintain that every child with a convulsion and fever should be sent to hospital for the establishment of the diagnosis—certainly if it is the first fit with fever. Many forget that fever may precipitate fits in epileptics, and that any severe major convulsion may cause a rise of

temperature. In either case the proper treatment for epilepsy should be instituted. Many forget the criteria for the diagnosis of febrile convulsions, diagnosing a mere febrile fit when in fact the true diagnosis is epilepsy. The worst mistake of all is to ascribe a convulsion to teething. Hardly a week passes without our seeing errors in the diagnosis of febrile fits, and many of these mistakes have tragic consequences.

What some of us are afraid of is missing a pyogenic meningitis. All paediatricians know that the infant with pyogenic meningitis may have no neck stiffness and no bulging of the fontanelle. All of us have seen numerous infants with late pyogenic meningitis who have been thought to have had a febrile fit or to be merely teething. The result of the delay in diagnosis may mean death or permanent sequelae, both of which could have been avoided if the child had been sent into hospital immediately he had a fit.—I am, etc.,

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Oral Contraceptives and Thromboembolic Disease

SIR,—In reply to a letter from two of us (21 December 1968, p. 770) suggesting that heavy cigarette smoking and use of oral contraceptives might interact in the pathogenesis of thromboembolism, Dr. M. P. Vessey and Dr. Richard Doll (14 June, p. 651) state that it seems more probable that the association of cigarette smoking and use of oral contraceptives among thromboembolic patients was due either to an extreme effect of chance or to a sociological effect no longer present. Drs. Vessey and Doll suggested the possibility that oral contraceptives were more likely to be used by women who also smoked cigarettes, but that the association has disappeared as the use of the preparation has become more general.

However, we had already retabulated the original data of Drs. Vessey and Doll¹ to indicate the lack of association between the use of oral contraceptives and cigarette smoking in the control patients. Moreover, similar retabulation of their more recent data (14 June, p. 651) confirms the lack of the association between the use of oral contraceptives and cigarette smoking in the control patients.

TABLE I.—Relative Incidence Rates of Thromboembolism by History of Cigarette Smoking and Oral Contraception*

Oral Contraceptives	No. of Cigarettes Smoked per Day			
	0	1-14	15+	Total
Not using ..	1†	1.5 × I	1.5 × I	1.2 × I
Using ..	7.2 × I	3.9 × I	22.7 × I	7.8 × I
Total ..	1.7 × I	1.9 × I	3.7 × I	2.1 × I

* Based on the history of cigarette smoking and oral contraception by 84 thromboembolic patients and 168 control patients, 1964-7.

† I = Incidence rate of thromboembolism among those who were not smoking cigarettes or using oral contraceptives.

In our letter we provided evidence for the possible potentiating effect of smoking on any aetiological role of oral contraception in

the pathogenesis of thromboembolism. Such potentiating effect is again suggested by merging the data from the two studies just referred to by Drs. Vessey and Doll.

Taking the combined data of Drs. Vessey and Doll at face value, we note that users of oral contraceptives who were also heavy smokers had an incidence of thromboembolism twenty-three times greater than those who neither used oral contraceptives nor smoked cigarettes (Table I). Again, combining their data and comparing the proportion of heavy smokers among users of oral contraceptives in thromboembolic and control patients, we find a difference that would occur by chance about once in fifteen times (Table II).

TABLE II.—Relative Distributions of Heavy Smoking Among Users of Oral Contraceptives in Thromboembolic and Control Patients*

Users of Oral Contraceptives	No. of Cigarettes Smoked per day		
	0-14	15+	Total
Control patients ..	20	3	23
Thromboembolic patients ..	26	16	42
Total ..	46	19	65

Sources of basic data: Vessey, M. P., and Doll, R. (1968 and 1969).

* Using the Yates correction, the Chi-square equals 3.3 indicating a probability of chance occurrence between 0.05 and 0.10.

Before we draw any firm conclusions concerning the significance of any interactions between cigarette smoking and oral contraception we would want to observe larger samples of thromboembolic and control patients. But the available data can hardly be used to rule out the possibility of a potentiating effect of cigarettes on any aetiological role of oral contraceptives in the pathogenesis of thromboembolism.—We are, etc.,

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REFERENCE

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Inappropriate Lactation

SIR,—The syndrome of inappropriate lactation or non-puerperal galactorrhoea has many causes.^{1,2} We report here a case of a young unmarried woman in whom the onset of lactation appeared to follow withdrawal of Metrolen M (ethynodiol diacetate with mestranol).

The 20-year-old patient was admitted as an emergency in April 1969 with retention of urine. Two years previously she had been diagnosed as suffering from multiple sclerosis, and since then had been seen on five occasions with exacerbations of the disease, the last three being in the previous December, January, and March. During these episodes she had received short courses of oral prednisone with good response. Because of increasingly severe dysmenorrhoea, Metrolen M was started in November 1968 and had been taken regularly on a 28-day cycle since. During the last three withdrawal bleeds the patient had experienced transient breast discomfort. The only other drug taken was diazepam, 10 mg. t.d.s., which had been taken for

the preceding nine months. The patient was mildly Cushingoid with evidence of multiple levels of involvement by the demyelinating process in the spinal cord and brain stem. Her presenting symptoms on this occasion were interpreted as being due to a high cervical plaque of demyelination causing a spastic bladder and sensory ataxia.

The most recent cycle of Metrulen M had finished the day before admission, and in view of the three relapses of the multiple sclerosis since she started taking the drug it was not recommenced. The patient was started on prednisone, 60 mg. daily. On the seventh admission day, in addition to increasing breast tenderness, discharge from her nipples was noticed. The breasts were tender and turgid, and a milky white discharge could be expressed with ease. Examination of this fluid confirmed the presence of fat globules. Since then the patient's neurological deficit improved significantly with prednisone, and the lactation gradually diminished and finally ceased after a period of one month. It had not recurred at the time of the most recent follow-up a further month later.

Many drugs may produce inappropriate lactation, the commonest offenders being the phenothiazines.¹⁻³ We have been able to find only two previous reports of a progestogen-oestrogen combination, in the form of a contraceptive pill, causing lactation.^{5,6} Neither diazepam nor prednisone have been reported as causing this. Disturbance of afferent pathways to the hypothalamus due to periventricular demyelination, known to be common though often asymptomatic in severe multiple sclerosis, would have to be considered as a possible mechanism in this patient. However, the dose relationship in time between stopping the Metrulen M and the onset of galactorrhoea, as in the case of Schachner,⁶ particularly in view of the previous breast changes associated with withdrawal bleeding, seemed to us to be strongly suggestive of a cause and effect relationship.—We are, etc.,

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Sugar and Ischaemic Heart Disease

SIR,—Mr. R. W. Howell and Dr. D. G. Wilson (19 July, p. 145) failed to establish any real difference in intake of sugar in patients with ischaemic heart disease and those free from such disease.

I wonder if they would have found a difference if their questionnaire had been somehow directed at the consumption of sugar from birth onwards, especially as it has been shown¹ that when the state of the coronary arteries of teenagers were looked at those who had no breast-feeding had mainly abnormal arteries, whereas most of those breast-fed for over two months had normal arteries.

It is my experience that the majority of bottle-fed babies have cane sugar added when their feed is made up.—I am, etc.,

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REFERENCE

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Methoxyflurane for Obstetric Analgesia

SIR,—Professor W. W. Mushin and his colleagues are performing a notable service in introducing—by way of well-composed, scientifically appraised studies—methoxyflurane into the field of obstetric analgesia. The topic of pain relief during labour tends to provoke lengthy discussion characterized by much subjective and emotional bias. Rather than indulge in an essay-type commentary on the three latest papers from Cardiff (2 August, pp. 255, 259, and 263)—which I am sure your columns would not sustain—may I fairly briefly make the following comments?

The validation of the objective method of assessment carried out under controlled conditions is not quite as clear-cut as the authors claim. According to Table V in the first paper (p. 255) in the recent trio maternal assessment (the ultimate criterion, as Professor Mushin and his colleagues correctly state) of the value of nitrous oxide and of methoxyflurane showed the latter to provide significantly more satisfactory relief from pain. In the field trial (p. 263) Table III shows that no significant difference was observed. The contrast is, of course, not surprising; in the "objective method study" the anaesthetist was periodically varying the concentration of administered agent in order to achieve optimum conditions, whereas in the field trial the concentration of inhaled drug was constant throughout. Thus, all that the "objective method" could do (and certainly it must not be decried because of this limitation) was to indicate that methoxyflurane is potentially in the same class as nitrous oxide as an inhalational analgesic. It is "in the field" where the real crunch comes; when there is no anaesthetist twiddling the knobs to provide a tailor-made concentration for the individual patient; where the "strong personal opinions" of the midwives are involved; where the size of the groups to be compared will ensure that there will be true equating out of inconstants such as individual emotional and cultural characteristics, idiosyncrasies of upbringing, previous medical and obstetric experience, and so forth (insufficient matching of these variables might have provided a serious flaw in the "observer" trials).

According to the results of the field trial, the one real advantage displayed by methoxyflurane (and of trichlorethylene) over nitrous oxide (50%) was that the midwives considered that the latter was a less efficient analgesic. In the opinion of the mothers there was virtually no difference in the pain-relieving efficiency of the three drugs; in the opinion of the midwives methoxyflurane induced significantly more unco-operativeness than did either of the other two agents. One is indeed left wondering: why pursue the matter further, unless cost or ease of transport counts heavily in favour of meth-

oxyflurane? Would it not be preferable to seek some other agent or technique which would not leave 20–30% of the mothers totally unrelieved, or only slightly relieved, of the pain of labour? Alternatively, how about a concentrated investigation (it would of necessity have to be retrospective) of the failures in an attempt to discover why they did not obtain relief?

The matter of the pethidine-induced neonatal depression—or, rather, the authors' comments upon it—deserves mention. I think it is fair to ask whether or not, in the Cardiff region, the use of narcotic antagonists (given in combination with pethidine or when appropriate, shortly before delivery or directly to the neonate) is advocated and practised. If not, is it intended that the policy be changed?

Finally, I must take direct issue with the opinion expressed in the concluding paragraph (p. 267) of your contributors' third paper. If the investigation is to be pursued in the admirably controlled manner in which it has so far been conducted by Professor Mushin and his colleagues the time is not yet ripe for the widespread, unsupervised use of methoxyflurane in obstetrics, for one outstanding reason. We have been provided with no information regarding the possibility that neonatal depression might result from long-protracted administration of this drug. In all three trials reported the mean duration of methoxyflurane administration was about 90 minutes, with a maximum of approximately one hour longer. I doubt that the numbers of cases involved in the "objective trials" were sufficient to enable an analysis of a possible correlation between neonatal depression and the length of time the agent was inhaled, and in the field trial analysis will be complicated by other factors such as obstetric pathology. However, as the authors have pointed out, the tissue level of concentration of methoxyflurane in a mother inhaling the drug intermittently in labour is cumulative—it will be so in the infant also (as, of course, is the case with trichlorethylene too—one reason perhaps why midwives are not greatly fond of using this agent except towards the end of labour).

Before encouraging an *ad lib.* trial of methoxyflurane we must surely learn more about the extent of its likely effect upon the infant, and especially so in respect of cases in which the foetus is already suspected to be at risk because of placental insufficiency. As a personal aside, may I say that I encourage midwives to let their patients begin to use the Entonox quite early in labour, and not merely as the end of the first stage approaches. I would be sorry to see any encouragement given to the tendency to reserve intermittent inhalational analgesia for the end of the first stage/second stage/delivery.—I am, etc.,

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Aluminium Hydroxide and Osteomalacia

SIR,—In common with the osteomalacia arising from disorders such as steatorrhoea, chronic renal failure, and in the post-gastrectomy state, that which originates from the ingestion of excessive quantities of aluminium hydroxide (2 August, p. 287) may be attended by hyperplastic changes in the parathyroid glands induced by the low serum levels of